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Preface

Pulmonary toxicology, as a recently emerged subspecialty of occupational medicine, exists almost entirely because of the changing state of our industrialized civilization. Without our modern way of life, most of the problems which we associate with pulmonary toxicology would disappear. It may be that, with an understanding of disease processes and wise management of our environment, pulmonary toxicology could return to obscurity; however, current trends indicate that the significance of pulmonary toxicology will continue to increase as we devise new ways to administer our resources.

Pulmonary diseases caused by agents in our environment have existed for centuries, although the complexity and extent of the problem has never been as great as it is today. Pneumoconioses of inhaled particles have occurred for as long as men have quarried stone for construction purposes. Association of diseases with certain occupations was clearly described by Ramazzini in his famous *De Morbis Artificum* published in 1713. The Industrial Revolution increased demands for coal, iron and other commodities, and with those increases came increases in pulmonary disease. The increase in pulmonary disease during the last century was primarily associated with increased utilization of resources. Today, the problem of environmentally related pulmonary disease is much more complicated because, in addition, we have new agents constantly being introduced into our living and working environments. New toxicants reach the lungs not only through the air we breathe but also through the circulation. New construction materials, plastics, gasoline additives, insecticides, food additives, drugs, solvents, paint sprays, deodorant sprays, cosmetics—all contribute to a new order of problems in pulmonary toxicology. The list of new compounds and agents with which the lungs must deal is enormous, and yet in very few cases have studies been made on the interactions between those agents and the lungs. Will we be as unprepared for debilitating pulmonary disease resulting from our industrial revolution as were those victims of the first Industrial Revolution?

The primary function of the lung as a gas exchange unit is well understood. Because the lung has such a large surface area and because such large volumes of air experience its surface, the lung is, in fact, the major interface between an organism and its environment. To accommodate this relationship, the lung is extremely complex and is subject to stresses experienced by no other organ. Only through the multidisciplinary approach of modern scientific research have we begun to understand the depth of that complexity. In this monograph and the one to follow (Methods in Pulmonary Toxicology, EHP, Volume 56), I have attempted to define this multidisciplinary approach to pulmonary toxicology as it exists within the laboratories of researchers recognized as authorities in their fields. These monographs are intended as a consolidation of the discipline, thus allowing access to problems peculiar to the lung and identification of problem areas in need of attention. In planning these monographs I have included problem areas, both old and new, as well as areas whose involvement in pulmonary toxicology are only beginning to be realized. For example, the immune system of the lung is poorly understood although it is clearly a primary factor in the manifestation of several lung diseases. Mechanisms which underlie immunologic lung diseases such as hypersensitivity pneumonitis are not known. Collagen and elastin biosynthesis are of utmost importance to the lungs and are significant factors in pulmonary disease processes but the cellular and molecular mechanisms which regulate and control these systems are obscure. The surfactant system is critical for the maintenance of pulmonary functions but its significance as a target for toxic agents has yet to be fully appreciated, and its possible role in protecting the lung against the action of fibrogenic dusts is a new and potentially important aspect which has received very little attention. I was very fortunate in having the manuscript on mechanisms of pulmonary fibrosis by Richards and Curtis submitted for publication through normal channels. It was not intended to be part of this monograph but the subject matter fitted into the basic theme so well that I succumbed to temptation and included it, although a distinction has been maintained. The discussion by Richards and Curtis concerning fibrogenic dusts, pulmonary surfactant, and protein crosslinks raises several novel ideas with potentially great significance in understanding the processes which lead to fibrosis. Many chemical agents give rise to pulmonary damage, but very little is known about the cellular and molecular mechanisms involved. What is the role of the mast cell in pulmonary toxicology? Prostaglandins appear to play a role in the control of pulmonary secretions and, therefore, could be crucial in counteracting the toxic effects of inhaled agents. The lungs are not without defenses as evidenced by the fact that it often takes years for pulmonary diseases to manifest themselves. These defenses, which include the xenobiotic metabolizing enzyme systems, alveolar macrophages and other phagocytic cells, particle clearance processes, and mech-

anisms through which cells are recruited from the circulation, are extremely important to the lungs and are some of the major factors which influence the pulmonary toxicology of chemicals and particles. However, the susceptibility of those defenses to toxic agents is in itself a subject which has been addressed only in part.

Much of pulmonary toxicology is associated with the anatomy and cellular variation within the lungs. Pathological studies account for the bulk of the literature and many of these studies are misleading in their descriptions. To overcome some of these problems, the first paper is devoted to the normal lung. The next several papers address the problems which arise from the interaction of chemical and particulate agents with the lung. At the subcellular level several biochemical systems have been identified as critical to the lung, and their role in pulmonary toxicology is discussed. Finally, pulmonary defenses and their relationships to pulmonary diseases are examined.

These papers are the concerted efforts of many people, all of whom I thank for their contributions, patience, and understanding.

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Editor